

AMENDMENT

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims:

1. (allowed) A method of site-specific delivery of therapeutic or diagnostic agent to a region of interest within a fluid-filled cavity, vessel, or fluid perfused tissue by ultrasound comprising the steps of:
 - a. introducing an agent-loaded microbubble population into said region of interest, said microbubble population having a controlled fragility characterized by a wall thickness to diameter ratio that defines a threshold power intensity value of ultrasonic energy where microbubble rupture occurs in the population,
 - b. applying an ultrasonic signal to the region of interest at a power intensity sufficient to induce microbubble rupture,
 - c. maintaining said power intensity until at least a substantial number of microbubbles are ruptured.
2. (allowed) A method according to Claim 1 comprising, prior to said step (b) the step of monitoring a location of said microbubbles within said cavity, vessel or tissue to detect the presence of said microbubbles at said region of interest.
3. (allowed) A method according to Claim 2, wherein said location of said microbubbles is monitored by applying an ultrasonic signal to the region of interest at a power intensity below a threshold power intensity value where microbubble rupture occurs.
4. (allowed) A method according to Claim 1, wherein said microbubble population is comprised of microbubbles having diameters within a range of about 1 to 10 microns.
5. (allowed) A method according to Claim 1, wherein said microbubble population is comprised of microbubbles having an outer shell comprising an outer layer of biologically compatible amphiphilic material and an inner layer of a biodegradable polymer.
6. (currently amended) A method according to Claim 4 5, wherein said amphiphilic material comprises a protein.

7. (currently amended) A method according to Claim ~~5~~ 6, wherein said protein comprises collagen, gelatin, albumin, or globulin, ~~or glycosaminoglycan~~.

8. (currently amended) A method according to Claim ~~4~~ 5, wherein said biodegradable polymer comprises polycaprolactone, polylactide, polyglycolide, polyhydroxyvalerate, polyhydroxybutyrate, or copolymers thereof.

9. (allowed) A method according to Claim 1 wherein said region of interest is a heart.

10. (allowed) A method according to Claim 1 wherein said region of interest is a kidney.

11. (allowed) A method according to Claim 1 wherein said region of interest is a liver.

12. (allowed) A method according to Claim 1 wherein said threshold intensity of ultrasonic power where microbubble rupture occurs is sufficient to provide a mechanical index between 0.1 and 1.9.

13. (allowed) A method according to Claim 1 wherein said ultrasonic power is produced by a plurality of transducers focused at said region whereby the intensity and wave superimposition at a point of convergence of the emitted ultrasonic beams is sufficient to rupture the microbubbles.

14. (allowed) A method according to Claim 1 further comprising ultrasonically monitoring the release of said pharmaceutical agent from the microbubbles to determine rate of release and cumulative dosage released by monitoring microbubble rupture.

15. (allowed) A method according to Claim 1 wherein said ultrasonic power is produced by a transducer embodied within a distal portion of a cannula to disrupt said microbubbles as they flow to said region.

16. (currently amended) A method according to Claim 1 wherein said ultrasonic power is produced by a transducer ~~implanted within a body~~ near said region.

17. (allowed) A method according to Claim 1 wherein said ultrasonic power is produced by a transducer affixed to an external, wearable object affixed near said region of interest.

18. (allowed) A method according to Claim 1 wherein said therapeutic agent is a drug to limit ischemic injury to a heart.

19. (allowed) A method according to Claim 1 wherein said therapeutic agent is a drug to limit reperfusion injury to a heart.

20. (allowed) A method according to Claim 1 wherein said therapeutic agent is a drug to limit restenosis of a coronary artery.

21. (allowed) A method according to Claim 1 wherein said therapeutic agent is a drug that comprises a fibrinolytic agent, vasodilator, calcium channel blocker, angiogenesis agent, anti-platelet agent, anti-white cell agent, endocardium acting agent, free radical scavenging agent, or anti-restenosis agent.

22. (currently amended) A method according to Claim ~~17~~ 21 wherein said drug comprises adenosine, adenosine monophosphate, adenosine diphosphate, adenosine triphosphate or chemical derivatives of adenosine.